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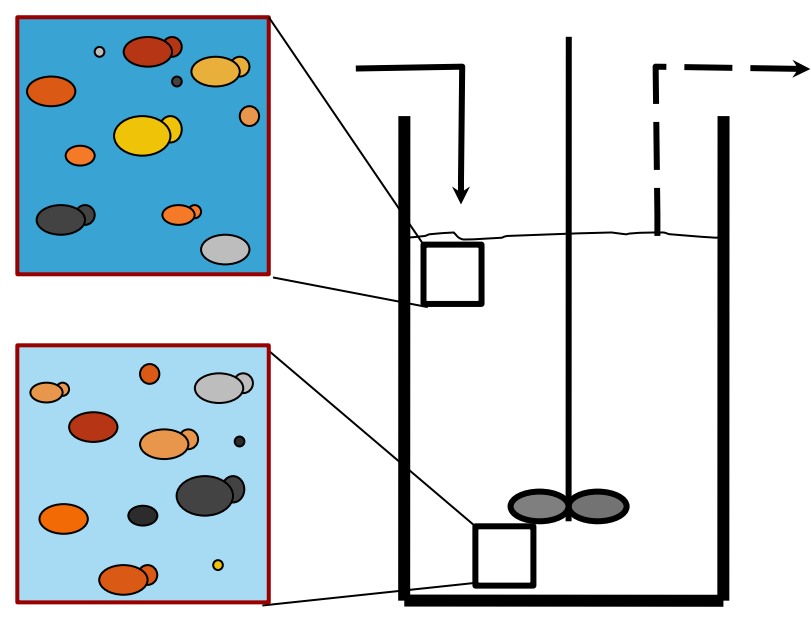
Multi-scale modelling for prediction of distributed cellular properties

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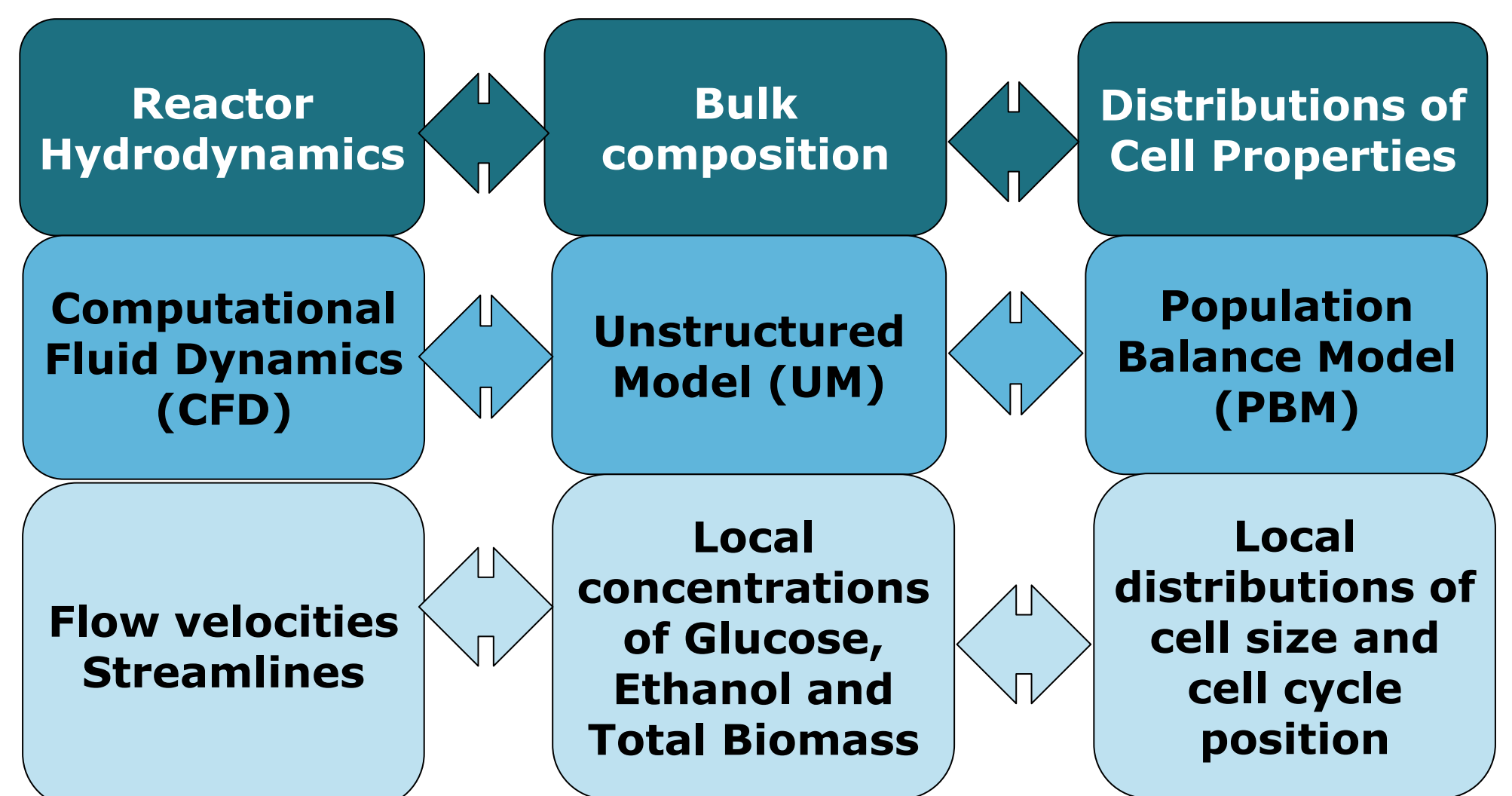


Studying the development of cell property distributions in the presence of spatial substrate gradients

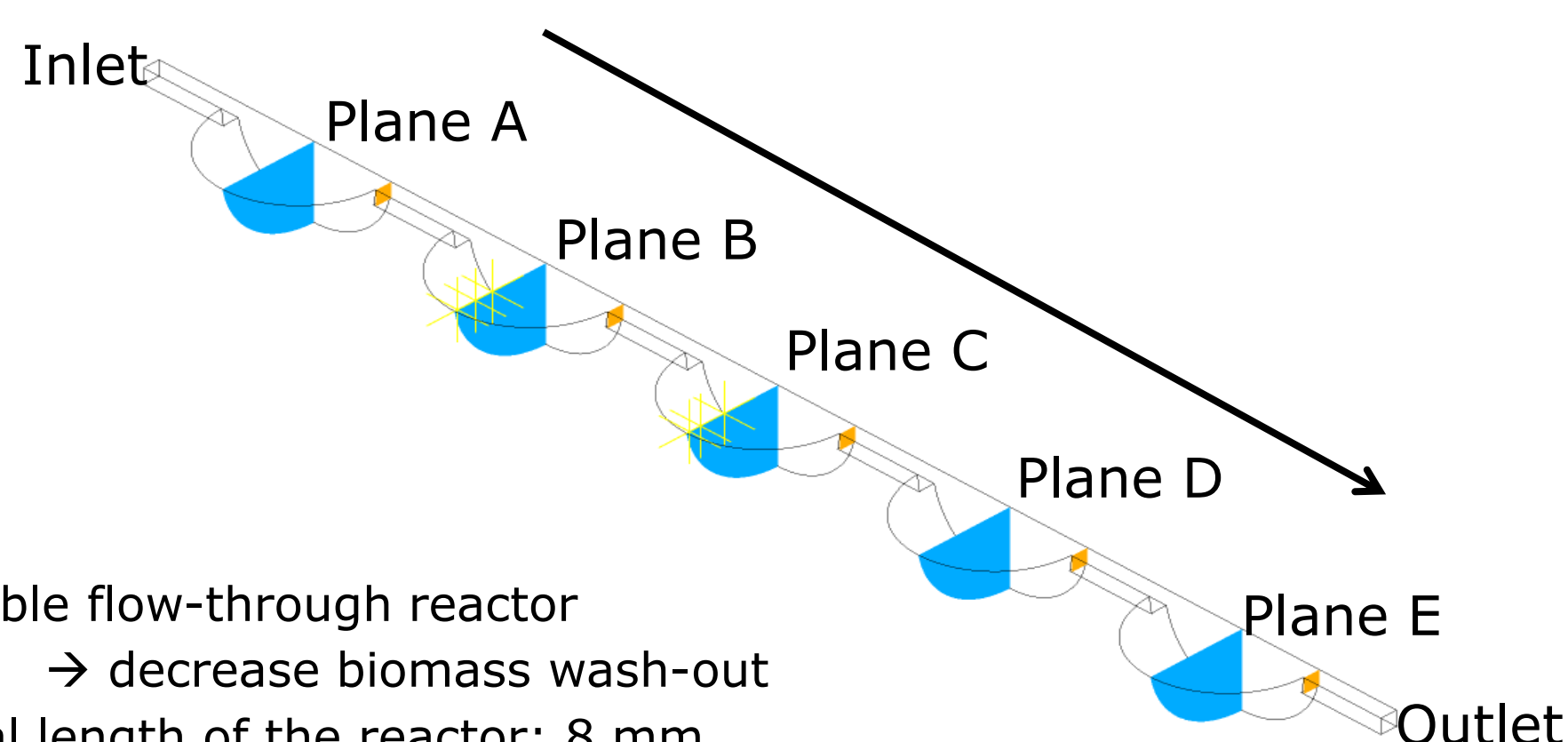
Non-ideal mixing

Substrate gradients

Enhance cell-to-cell variability

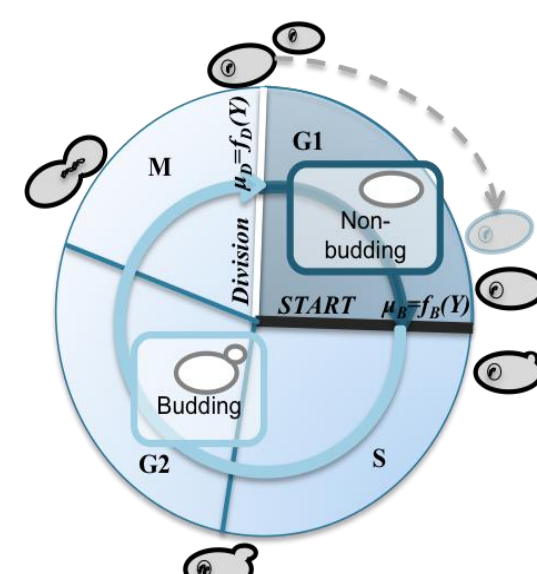


Case study: Microbioreactor



- Bubble flow-through reactor
→ decrease biomass wash-out
- Total length of the reactor: 8 mm
- Anaerobic growth of budding yeast
- Slow feed of glucose: 1 nL/s vs. 0.1 nL/s
- Laminar flow
- Incompressible fluids
- Diffusion is *not* taken into account
- Implemented in CFX 12.1 and the biological model was implemented using CEL language
- Hexahedral mesh with 32159 elements and 36535 nodes
- PBM discretized in 2x 20 pivots using the fixed-pivot method

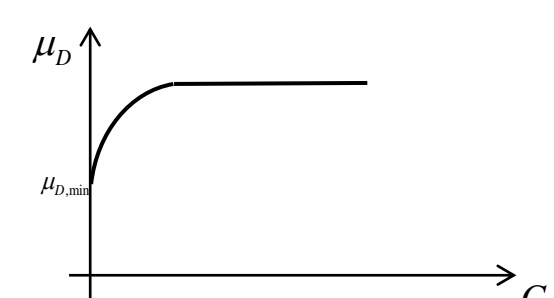
2-stage cell size structured PBM...



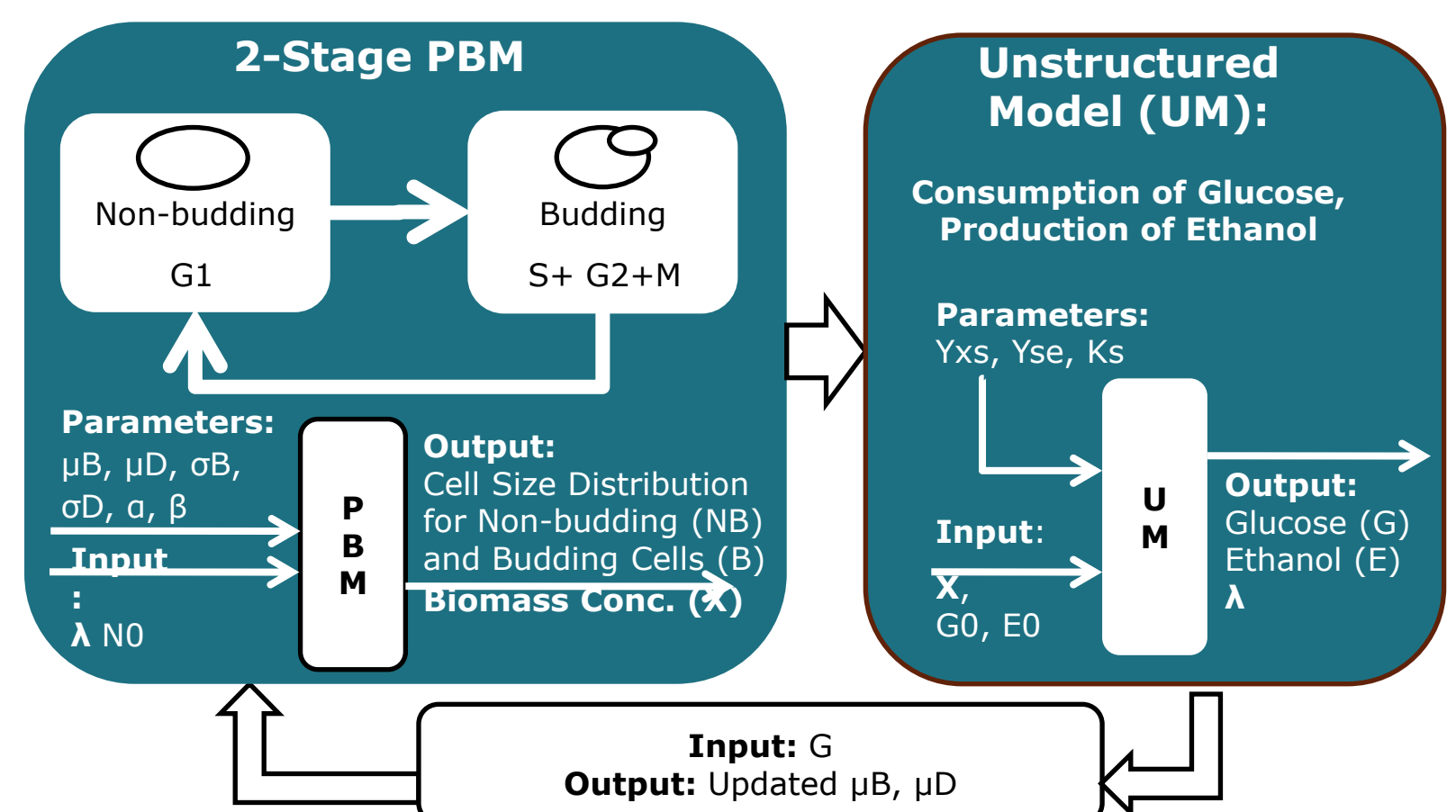
Critical Budding and Division Sizes as functions of the substrate concentration

$$\mu_B = k_B \frac{G}{G + K_{BG}} + \mu_{B,min}$$

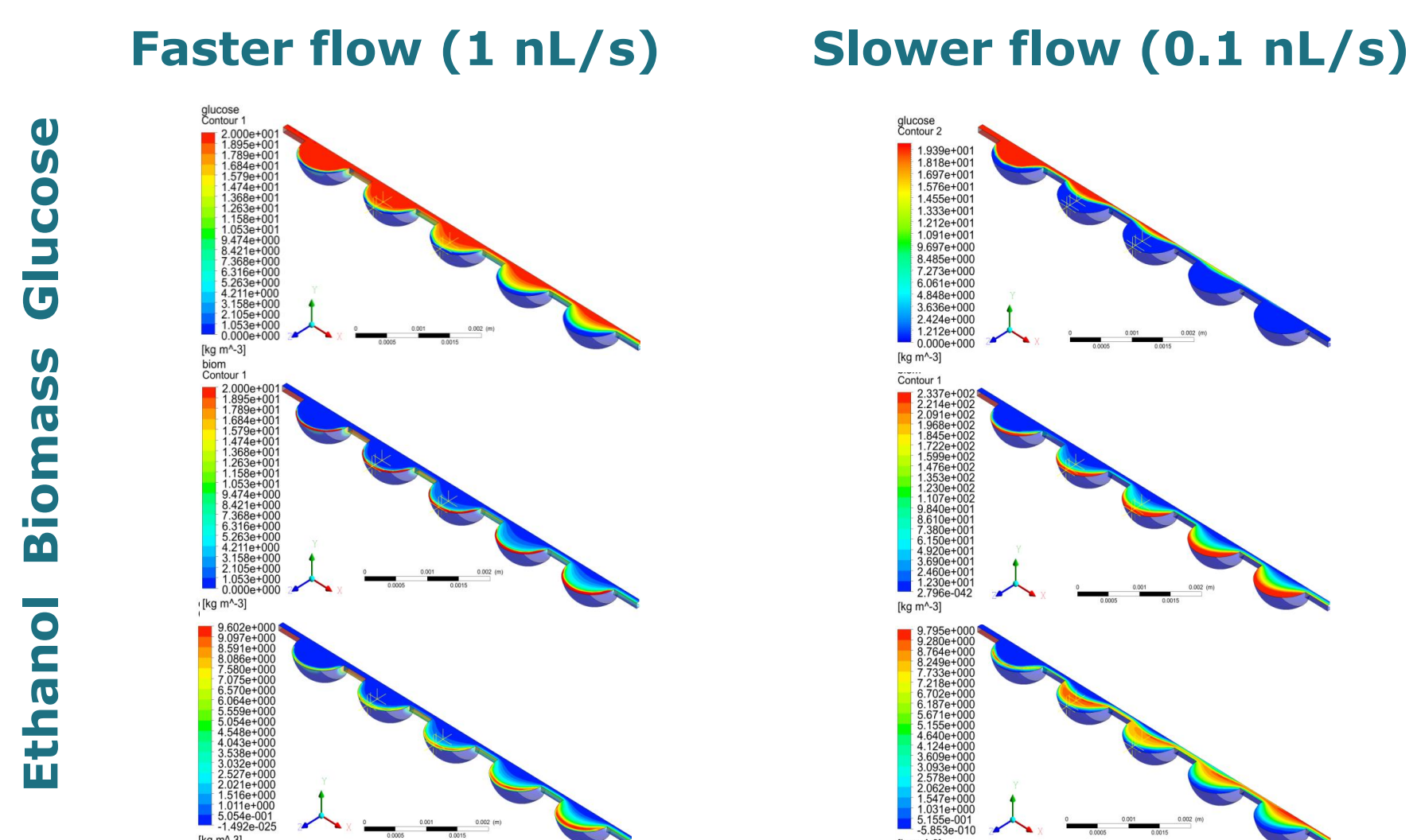
$$\mu_D = k_D \frac{G}{G + K_{DG}} + \mu_{D,min}$$



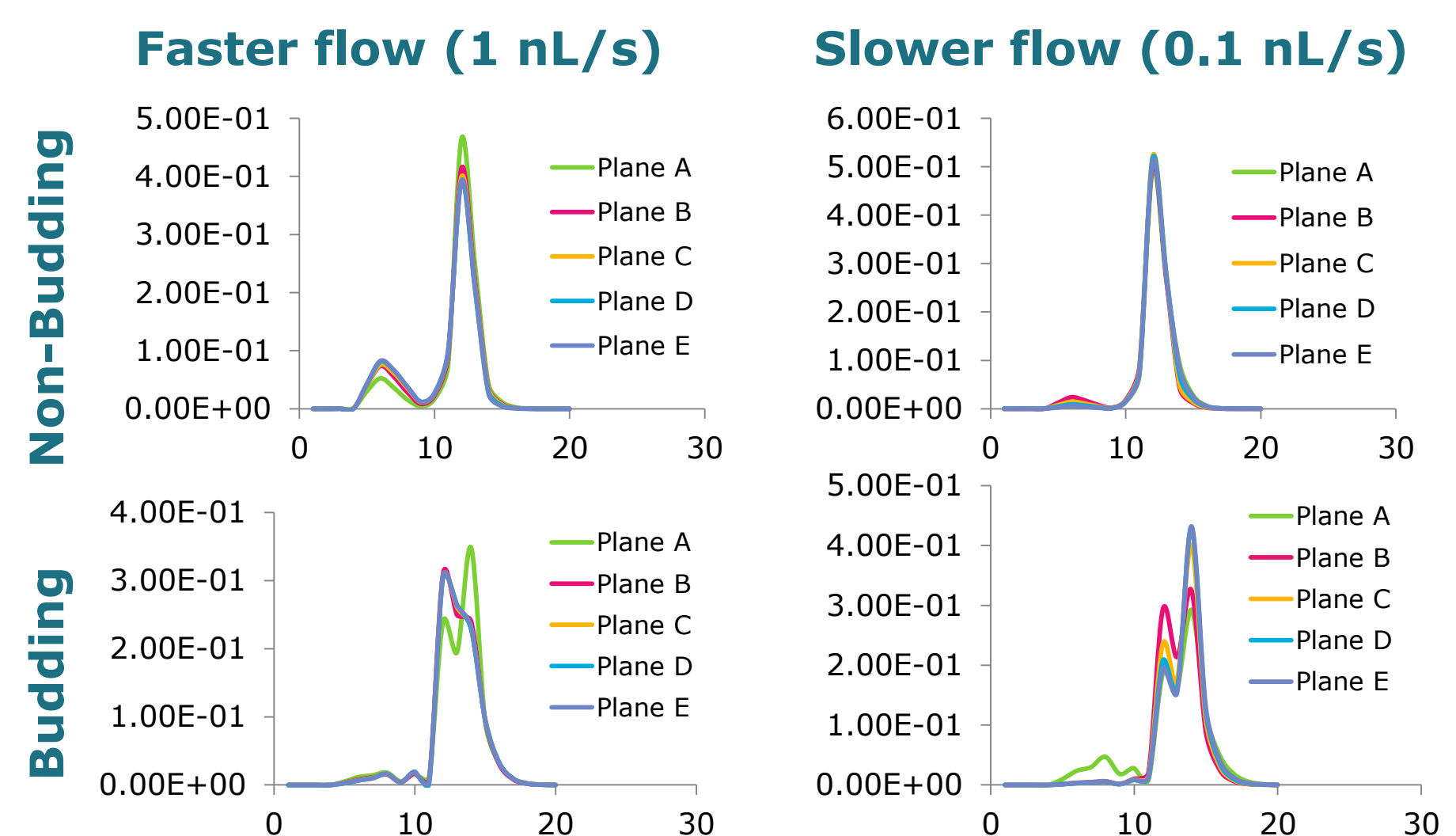
... coupled to an unstructured model



Concentration profiles



Local Concentrations and distributions



Conclusion & Outlook

- Challenge in understanding the local distributions as they result from the interplay of flow and the population dynamics
- Proof-of-concept of integration of a CFD and PBM for multi-scale biological applications.
- In silico* simulation of various scenarios: different flow conditions, cellular kinetics, etc.
- Experimental Validation: overall distribution of biomass, bulk concentrations and cell distributions at the outlet



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